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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/594,014	09/25/2006	Petrus Jacobus Dekker	ES/4662-335	3949
23117 7590 01/22/2009 NIXON & VANDERHYE, PC 901 NORTH GLEBE ROAD, 11TH FLOOR ARLINGTON, VA 22203			EXAMINER PAK, YONG D	
			ART UNIT 1652	PAPER NUMBER
			MAIL DATE 01/22/2009	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/594,014	DEKKER ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	YONG D. PAK	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 06 November 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-25 is/are pending in the application.
- 4a) Of the above claim(s) 1-9 and 22-25 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 10-21 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 16 June 2008 is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>9/25/06</u> .   | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

This application is a 371 of PCT/JP05/04392.

The amendment filed on November 6, 2008, amending claims 1 and 10, has been entered.

Claims 1-25 are pending. Claims 1-9 and 22-25 are withdrawn. Claims 10-21 are under consideration.

### ***Election/Restrictions***

Applicant's election with traverse of Group II (claims 10-20) with an election of SEQ ID NO:2 (*hdfA*) in the reply filed on November 6, 2008 is acknowledged. The traversal is on the ground(s) that Groups II and III should be examined together because the single general inventive concept of the invention is increasing the efficiency of targeted integration of a polynucleotide in a filamentous fungal cell by steering an integration pathway towards homologous recombination, which new, and modulating the expression of HR and/or NHR components (such as *hdfA* or *hdfB*) are special technical features linked by the single general inventive concept. Although Examiner disagrees with the single general inventive concept linking Groups II and III, Group III has been rejoined with Group II. The traversal is on the ground(s) that examination of all pending claims would not constitute a serious burden. This is not found persuasive because the instant application is a national stage application submitted under 35 U.S.C. 371 and unity of invention (not restriction practice pursuant to 37 CFR 1.141 - 1.146) is applied. Burdensome search is not a factor in determining unity of invention.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-9 and 22-25 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on November 6, 2008.

### ***Claim for Foreign Priority***

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

### ***Information Disclosure Statement***

The information disclosure statement (IDS) submitted on September 25, 2006 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

### ***Claim Objections***

Claim 21 recites "Method for". It appears that the article "A" is missing.

Appropriate correction is required.

Claim 18 recites "*Trichodermaspecies*". It appears that a space is missing between "*Trichoderma*" and "species".

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10-21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 10-21 are drawn to a mutant filamentous fungal, *Aspergillus*, *Penicillium*, *Trichoderma*, *Aspergillus niger*, *Aspergillus oryzae*, *Penicillium chrysogenum*, or *Penicillium citrinum* cell having a preference for NHR and having a decreased ratio of NHR/HR as compared to the wildtype of said cell, wherein said mutant **(A)** has any mutation, **(B)** is deficient in a gene encoding a component involved in NHR, has a decreased level of a component involved in NHR, gene involved in NHR has been replaced by a non-functional variant, or has an increased level of a component involved in HR, and **(C)** is deficient in its hdfA, hdfB, and/or homologues thereof, and a method of using said cell to produce a polypeptide of interest. Therefore, these claims encompass any all mutant filamentous fungal, any or all mutant *Aspergillus*, any or all mutant *Penicillium*, any or all mutant *Trichoderma*, *Aspergillus niger*, *Aspergillus oryzae*, *Penicillium chrysogenum*, or *Penicillium citrinum* cell having a preference for NHR and having a decreased ratio of NHR/HR as compared to the wildtype of said cell, wherein

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said mutant **(A)** has any mutation, **(B)** is deficient in any gene encoding any or all component involved in NHR, has a decreased level of any or all component involved in NHR, or any gene involved in NHR replaced by any non-functional variant, **(C)** is deficient in *hdfA*, *hdfB*, and/or any homologues thereof, and **(D)** has an increased level of any or all component involved in HR and a method of using said cell to produce a polypeptide of interest. Therefore, these claims are drawn to a genus of any or all mutant filamentous fungal, any or all mutant *Aspergillus*, any or all mutant *Penicillium*, any or all mutant *Trichoderma*, *Aspergillus niger*, *Aspergillus oryzae*, *Penicillium chrysogenum*, or *Penicillium citrinum* comprising **(A)** any mutation, **(B)** deletion/mutation of any gene involved in NHR, **(C)** deletion of *hdfA*, *hdfB* or homologues thereof and **(D)** an increased level of any component involved in HR, wherein said mutant cell has a decreased ratio of NHR/HR as compared to the wildtype of said cell. The specification describes a mutant *Aspergillus niger* and *Penicillium chrysogenum* comprising a deletion of its *hdfA* and/or *hdfB* genes, wherein said cells have a decreased ratio of NHR/HR as compared to the wildtype of said cell. However, the specification does not provide an actual reduction to practice of the claimed filamentous fungal, *Aspergillus*, *Penicillium*, *Trichoderma*, *Aspergillus oryzae*, or *Penicillium citrinum* cells because the specification fails to disclose the structure of *hdfA* and *hdfB* (or their homologs) genes in non- *Aspergillus niger* and *Penicillium chrysogenum* which must be known in order to delete/mutate said genes in the claimed filamentous fungal, *Aspergillus*, *Penicillium*, *Trichoderma*, *Aspergillus oryzae*, or *Penicillium citrinum* cells, which comprises any or all filamentous fungus, any or all *Aspergillus*, any or all *Penicillium*, any or all

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*Trichoderma*, *Aspergillus oryzae*, or *Penicillium citrinum*, wherein its *hdfA* or *hdfB* or homologs thereof are mutated or deleted. The specification does not disclose the isolation or cloning of any non-*A. niger* and non-*P. chrysogenum* *hdfA* or *hdfB* genes. The specification does not describe any structural features of non-*S. cerevisiae* GCY1 and YPR1 genes that would have been expected to be shared by other yeast or other filamentous fungal, *Aspergillus*, *Penicillium*, *Trichoderma*, *Aspergillus oryzae*, or *Penicillium citrinum* cells *hdfA* or *hdfB* (or homologs thereof) genes. The specification also does not describe any structural features of the claimed genus of filamentous fungus comprising an increased level of a component involved in HR. The level of knowledge and skill in the art does not allow those skilled in the art to structurally envisage or recognize any or all filamentous fungus, any or all *Aspergillus*, any or all *Penicillium*, any or all *Trichoderma*, *Aspergillus oryzae*, or *Penicillium citrinum* having a deletion or mutation of its *hdfA*, *hdfB* or homologs thereof or increased level of a component involved in HR because it is known that corresponding genes in different species tend to differ in sequence and the amount and type of sequence variation is unpredictable. Since the structure of *hdfA*, *hdfB* and homologs thereof would be expected to vary unpredictable from the structure of the *A. niger* and *P. chrysogenum* *hdfA* and *hdfB*, the disclosed *A. niger* and *P. chrysogenum* mutants comprising a deletion of its *hdfA* and *hdfB* do not constitute a representative number of species to describe the whole genus of any or all filamentous fungus, any or all *Aspergillus*, any or all *Penicillium*, any or all *Trichoderma*, *Aspergillus oryzae*, or *Penicillium citrinum* comprising a mutated or deleted *hdfA*, *hdfB* and/or homologs thereof and there is no

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evidence on the record of the relationship between the structure of the disclosed mutant *A. niger* or *P. chrysogenum* and the structure of any or all filamentous fungus, any or all *Aspergillus*, any or all *Penicillium*, any or all *Trichoderma*, *Aspergillus oryzae*, or *Penicillium citrinum* comprising a deletion or mutation of its *hdfA*, *hdfB* and/or homologs thereof. Because the disclosed *A. niger* and *P. chrysogenum* mutant having a deletion of its *hdfA* and *hdfB* are not representative of the entire claimed genus, and the specification does not disclose structural features shared by members of the genus, the description of the said mutant *A. niger* and *P. chrysogenum* having a deletion of its *hdfA* and *hdfB* would not have put the application in possession of the common structural attributes or features shared by members of the genus that structurally distinguish the members of the genus from other materials at the time of filing. Thus, the description of the *A. niger* and *P. chrysogenum* mutant having a deletion of its *hdfA* and *hdfB* is not sufficient to describe the claimed genus of any or all filamentous fungus, any or all *Aspergillus*, any or all *Penicillium*, any or all *Trichoderma*, *Aspergillus oryzae*, or *Penicillium citrinum* comprising a deletion or mutation of its *hdfA*, *hdfB* and/or homologs thereof. Accordingly, the specification does not provide a representative number of species or sufficient common structural features to show that the application would have been in possession of the claimed genus as a whole at the time of filing. Therefore, the specification fails to describe a representative species of the genus comprising any or all filamentous fungus, any or all *Aspergillus*, any or all *Penicillium*, any or all *Trichoderma*, *Aspergillus oryzae*, or *Penicillium citrinum* comprising a deletion or mutation of its *hdfA*, *hdfB* and/or homologs thereof.



Given this lack of description of the representative species encompassed by the genus of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the inventions of claims 10-21.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at [www.uspto.gov](http://www.uspto.gov).

#### ***Other Relevant Art***

Ninomiya et al. (reference OR in the IDS filed on September 25, 2006) discloses a filamentous fungus having a mutation of its *KU70* and *KU80* (homologs of *hdfA* and *hdfB*), wherein said mutant has a decreased NHR/HR ratio but is not available as prior art because the reference was published or made known to the public after the instant invention was filed.

Ivanov (US Patent 6,569,681 - reference AR in the IDS filed on September 25, 2006) discloses deleting *KU70* and *KU80* (homologs of *hdfA* and *hdfB*), wherein said mutant has a decreased NHR/HR ratio but is not available as prior art because the reference does not teach a *KU70* and *KU80* (homologs of *hdfA* and *hdfB*) of filamentous fungal cells that prefer NHR over HR.

***Conclusion***

None of the claims are in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

/Yong D Pak/  
Primary Examiner, Art Unit 1652